REMARKS

Claims 7 and 12-17 are pending and stand ready for further action on the merits. Claim 7 has been amended to recite that the crystals are of "unlabeled" mirtazapine hydrate. Support for the amendment of claim 7 can be found in the examples of the present specification. Applicants maintain that there is support for reciting that the presently claimed mirtazapine hydrate is "unlabeled" based on the examples in the present application. None of the examples are labeled and each example contains a naturally occurring quantity of the radioisotope. Applicants strongly contend that the mirtazapine hydrate of presently amended claim 7 which recites that the mirtazapine hydrate is "unlabeled" still retains a naturally occurring ratio of labeled isotopes.

No new matter has been added way of the above-amendment.

Issues Under 35 USC 102

Claims 7 and 12-15 are rejected under 35 U.S.C. § 102(b) as being clearly anticipated by Kaspersen et al. Applicants respectfully traverse the rejection.

Applicants note that the discussion and conclusions made during the August 12, 2003 Interview is relevant to this rejection. We now turn to the results of the Interview.

Interview

Applicants note with appreciation that Examiners Habte and Berch conducted a personal interview with Applicants' representative on August 12, 2003. This interview was very helpful in clarifying the issues.

On page 2 of the Interview Summary form, the Examiner characterizes the Interview as follows:

> In regard to the 102(b) rejection of claims 7, 12-15 (Paper No. 23, paragraph 3), applicants have proposed to add "unlabeled" to overcome the Kaspersen. The proposed language claim would overcome the 102(b) rejection and not introduce a description problem, but applicants still have to overcome the 103(a) rejection that replaces said 102(b) rejection.
>
> In regard to the 102(b) rejection of claims 16-17, applicants would present their argument in response to the final rejection (Paper No. 23).

Based on the results of the August 12, 2003 Interview, Applicants have hereinabove amended claim 7 to recite that the mirtazapine hydrate is "unlabeled" to overcome the rejection over Kaspersen et al. (J. Label. Comp. and Radiopharm., 27, No. 9, 1055, **1989**). The Examiner has taken the position that such an amendment would overcome the 102(b) rejection, and there would not be a written description problem. Accordingly, formal withdrawal of the rejection is respectfully requested.

In addition, the Examiner requests that Applicants clarify the reasons why the presently claimed unlabeled mirtazapine hydrate is not made obvious by Kaspersen et al. under 35 U.S.C. § 103. The following comments address this request by the Examiner.

Nonobviousness Of Claims In View Of Kaspersen et al.

It is apparent from the whole disclosure of the instant specification that the object of the present invention is to provide pharmaceuticals useful as antidepressant for therapeutic application (see, *inter alia*, page 1, lines 11-15 of the instant specification). In other words, the ultimate object of the present invention is to provide low hygroscopic crystals of mirtazapine useful as therapeutic agents, which are prepared by drying the crystals of a mirtazapine hydrate of inventive formula (I).

Accordingly, the crystals of a mirtazapine hydrate of inventive formula (I) are well suited as an intermediate for the antidepressant therapeutic agent which are low hygroscopic crystals of mirtazapine.

Kaspersen et al. disclose the preparation of labeled compounds. Kaspersen et al. also disclose that:

> "[f]or metabolic studies in animal and man and for the determination of the bioavailability, the compound labeled with ^{3}H, ^{14}C, and ^{13}C was needed."

Thus, it was an object of Kaspersen et al. to prepare the labeled compounds (see page 1055, item "INTRODUCTION"). In other

words, it is thought that the labeled compounds prepared by Kaspersen et al. are to be administered a single time for studies. There is no teaching or suggestion that the labeled compounds are continuously administrated to a patient as a therapeutic substance.

Also, there is clearly no need to use the labeled compounds as pharmaceuticals for humans, and there is no particular advantage disclosed in using the labeled compounds as a therapeutic substance. For example, the compound at page 1058, Fig. 4, which is pointed by the Examiner, is abbreviated as "[$^{13}C_6$]-Org 3770" and denoted as the number of the compound "1c". Also, the compound at page 1067 is abbreviated as "[10-^{14}C]-Org 3770" and denoted as the number of the compound "1d".

Simply put, Kaspersen et al. teach the preparation of these labeled compounds for use in metabolism studies. As such, there would be no motivation to modify the labeled compounds of Kaspersen et al. to use them in treatment. Applicants submit that the mere fact that the claimed invention is within the capabilities of one of ordinary skill in the art is not sufficient by itself to establish *prima facia* obviousness. The prior art must contain a suggestion to make the modification, and there is clearly no suggestion by Kaspersen et al. to make the modifications. The mere fact that a prior art device or process could have been modified, does not make the modification obvious unless the prior art suggested the desirability of the modification. See e.g., In re

Gordon, 221 USPQ 1125, 1127 (Fed. Cir. 1984) and Ex parte Tanksley, 37 USPQ2d 1382 (BPAI 1994).

Regarding the inventions of claims 14 and 15, drying of the crystals of the mirtazapine hydrate is efficiently carried out because the crystals are previously pulverized to an average particle diameter of 10 to 70 μm, preferably 20 to 60 μm (see page 9, lines 1-4 of the instant specification). However, Kaspersen et al. fail to teach or suggest this drying step. Therefore, the claimed invention according to claims 14 and 15 was not fairly suggested by Kaspersen et al.

In view of foregoing, Applicants respectfully submit that the presently amended claims contain significant patentable distinctions from Kaspersen et al.

Van der Burg et al. U.S. Patent 4,062,848

Claims 16 and 17 are rejected under 35 U.S.C. § 102 (b) as being anticipated by Van der Burg et al. Applicants respectfully traverse this rejection.

In support of the rejection, the Examiner comments as follows:

> Van der Burg et al. teaches the pharmaceutical formulation of mirtazapine compounds on column 1 (line 7). Water solutions are one of the known formulations for pharmaceutical composition. Applicants claim pharmaceutical compositions of mirtazapine adduct that is the same as Van der Burg et al. Since a hydrate of mirtazapine in aqueous solution is a pharmaceutical composition and would be identical to a solution from the non-hydrate mirtazapine, the same material is obtained.

Based on the Examiner's comments given above, it appears that the Examiner is rejecting the inventive claims based on the pharmaceutical formulation of mirtazapine compounds. Applicants respectfully submit that inventive claims 16 and 17 are each drawn to a **method** for treating a human suffering from depression. Accordingly, inventive claims 16 and 17 are not pharmaceutical formulation claims, *per se*.

Furthermore, Applicants note that Van der Burg et al. teach certain tetracyclic compounds for use as antihistamines. Since Van der Burg et al. fail to teach or fairly suggest using a tetracyclic compounds to teach depression, as presently claimed.

As the MPEP directs, all the claim limitations must be taught or suggested by the prior art to establish a *prima facie* case of anticipation. See MPEP Section 2131. Since Van der Burg et al. fail to teach or fairly suggest using tetracyclic compounds to treat depression, a *prima facie* case of anticipation does not exist. As such, withdrawal of the rejection is respectfully requested.

Drawings

On the Office Action Summary Form (PTO-326) dated March 14, 2003, the Examiner indicates that the drawings are objected to by the Examiner. Applicants filed a Letter to the Official Draftsperson on April 24, 2003 which included formal drawings. Applicants respectfully request that the Examiner indicates whether the drawings submitted April 24, 2003 sufficiently address the objection to the drawings.

Conclusion

In view of the above amendments and comments, Applicants respectfully submit that the claims are in condition for allowance. A Notice of such fact is earnestly solicited.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Garth M. Dahlen, Ph.D. (Reg. No. 43,575) at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

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